REMARKS

Applicants' representative notes that the Office Action states that "[t]here is no information disclosure statement (IDS) with this application." However, an IDS was filed on February 27, 2008, which was acknowledged as received by EFS on said date (copies of the EFS Acknowledgment Receipt, Form 1449, and Statement Letter are provided herewith). Therefore, Applicants request that the IDS, including the accompanying documents, be considered.

Applicants respectfully request entry of amendments to claims 1, 3-10, 12, 13 14, 16, 22, and 50. Please cancel claims 9, 15 and 22, and withdraw claims 2, 11, 17-21, 23-49, and 51-56, without prejudice or disclaimer. Please add new claims 57-59 which further clarify particular nucleic acid or amino acid sequences for the glycoprotein of the invention. Support for the amendments can be found throughout the specification, including paragraphs [0039], [0043], [0049], [0184], [0237], Example 4, and the originally filed claims and, therefore, do not add new matter.

Applicants submit that pending claims 1, 3-10, 12-14, 16, 22, and 50 are in condition for allowance, and respectfully request that the claims as amended be entered.

Objections

Applicants have provided herewith corrections to claims 1, 4-9, 12, 13, 14, 22, and 50 as suggested in the Office Action.

For these reasons, Applicants respectfully request that the objections be withdrawn.

Rejection Under 35 U.S.C. §101

Claims 1, 9, and 12-15 stand rejected under 35 U.S.C. §101, as allegedly being directed to non-statutory subject matter. As claim 15 has been canceled, the rejection as applied to this claim is rendered moot.

Applicants traverse the rejection, as applied to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges that because the claims recite "A ---- chondroitinase glycoprotein" or "A polypeptide," the claims read on naturally occurring polypeptides.

As amended, none of the claims presently recite "A polypeptide" in the preamble, so this aspect of the rejection is rendered moot. Further, the claims recite "A substantially purified glycoprotein," not simply "A chondroitinase" or "A protein". The term "substantially purified," which modifies "chondroitinase," would be interpreted to involve the "hand of man" since the specification clearly recites that the term means "sufficiently homogenous to appear free of readily detectable impurities as determined by standard methods of analysis" (see paragraph [0125]). Applicants respectfully submit that the enzyme certainly does not exist in nature in the condition as defined. Moreover, the use of this term in the preamble is typical of claim construction in the chemical and biotechnology arts. For example, a database search of issued U.S. patents on the USPTO website using "substantially purified" limited to "aclm" results in 851 hits. As such, the use of the term does not, *per se*, make the claimed subject matter non-statutory.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1, 4-9, 12-15, 22, and 50 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. As claims 9, 15 and 22 have been canceled, the rejection as applied to this claim is rendered moot.

Applicants traverse the rejection as applied to the amended claims, including claims dependent therefrom, for the reasons given below.

Applicants submit that as the Court stated in Exxon Research & Engineering Co. v. United States, 20 U.S.P.Q.2d 1272 (Fed. Cir. 2001):

> "We have stated the standard for assessing whether a patent claim is sufficiently definite to satisfy the statutory requirement as follows: If one skilled in the art would understand the bounds of the claim when read in light of the specification, then the claim satisfies section 112 paragraph 2." (citations omitted).

The specification clearly provides a definition of the term at issue in paragraph [0125], and it is axiomatic that an Applicant may be his own lexicographer (see, M.P.E.P. §2173.01). While it is true that "substantially" is a broad term, its use does not make the claim indefinite *per*

se (see, e.g., In re Nehrenberg, 126 USPQ 383 (CCPA date)), and Applicants respectfully submit that the "breadth of a claim is not to be equated with indefiniteness." In re Miller, 169 U.S. P.Q. 597 (CCPA 1971). Further, because such a phrase does not stand in a vacuum, when read in light of the specification the skilled artisan would understand the scope of the phrase in view of the definition provided (see, e.g., In re Mattison, 184 USPQ 484 (CCPA date)). Moreover, as stated above, the term "substantially purified" is a tem of art (i.e., a database search of issued U.S. patents on the USPTO website using "substantially purified" limited to "aclm" results in 851 hits), and as such, one of skill would understand the metes and bound of the claims.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Rejections Under 35 U.S.C. §112, First Paragraph

Claims 1, 4-9, 13, and 50 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description support. Claim 9 has been canceled without prejudice and therefore the rejection is moot with respect to this claim.

Applicants traverse the rejection as applied to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that the specification does not support the genus as claimed. Applicants respectfully submit that such allegations are incorrect.

The position taken in the Office Action in view of the cited case law is inapposite in that none of the cases recited in the Action support a written description standard which requires a re-description of what was already known. For example, in University of California v. Eli Lilly and Co., 43 U.S.P.Q.2d 1398, at 1406 (Fed. Cir. 1997), the sequences encoding the cDNA at issue were *unknown*, where the court viewed that the naming of a member of a genus was not a proper basis for a claim to the entire group. In Fiers v. Revel, 25 U.S.P.Q.2d 1601, 1604, 984 F.2d 1164, at 1171 (Fed. Cir. 1993), much of the DNA sought to be claimed *was of unknown structure*, whereby the court viewed the breadth of the claims as embracing a "wish" or a research plan. Further, in Amgen Inc. v. Chugai Pharmaceutical Co., Ltd., 18 U.S.P.Q.2d 1016, 1021, 927 F.2d 1200, at 1206 (Fed. Cir. 1991), the court explained that *a novel gene* was not adequately characterized by its biological function alone because such a description would

represent a mere "wish to know the identity" of the novel material. Moreover, in Fiddes v. Baird, 30 U.S.P.Q.2d 1481, at 1483 (Bd. Pat. App. & Int. 1993), the court explained that the state of the art at the time the invention was filed, where the inventor only disclosed an amino acid sequence and *a theoretical DNA sequence*, there was inadequate knowledge concerning the relationship between gene structure and proteins for the theoretical sequence to be used to establish possession. For the instant invention there are no theoretical sequences, and both the amino acid sequences and nucleic acid sequences encoding them were already known, including recognized structure/function relationships. Thus, the present facts are distinguishable.

On the other hand, in Capon v. Eshhar, 76 U.S.P.Q.2d 1078, 1085, 418 F.3d 1349, at 1357 (Fed. Cir. 2005), the court concluded that requiring sequences to be fully presented, although the sequences are known, is an inappropriate generalization. The court reasoned that when the prior art includes sequence information, there is no *per se* rule that the information must be determined afresh. Id. In view of Capon, Applicant submits that the requirement that polypeptides prepared from known sequences of known function must be analyzed and reported in the specification is not the standard for written description. Id.

The claims as presently recited describe a genus of enzymes where the sequences and functions are defined and well known in the art (i.e., since at least 1999; see, e.g., Csoka et al., Genomics (1999) 60(3):356-361). As such, one of skill in the art could envision the structures of the chondroitinase glycoprotein (CHASEGP) of the claimed invention, and would appreciate that the inventors were in possession of the genus as claimed at the time the invention was filed.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Claims 1, 4-9, 12, 13, 15, 22 and 50 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. As claims 9,15 and 22 have been canceled, the rejection as applied to this claim is rendered moot.

Applicants traverse the rejection as applied to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that the specification is not enabling for "any chondroitinase glycoprotein having any structure or any chondroitinase glycoprotein having any

catalytically active portion thereof or any polypeptide having chondroitinase domain, wherein the encoded nucleic acids hybridize under high stringency conditions at least 70% of its full length of nucleotides 726-1996 in SEQ ID NO: 3 or SEQ ID NO: 5 or at least any one domain thereof or any catalytically active portion of the domain and a compositions comprising any chondroitinase glycoprotein having any structure."

While Applicants do not acquiesce to the reasoning offered in the Office Action, the claims have been amended such that any (and all) chondroitinase glycoproteins (i.e., CHASEGPs) are not embraced by the claims. As amended, the claims recite that the CHASEGPs are mammalian and comprise a HYAL4 polypeptide which is truncated at the C terminal residue relative to the endogenous GPI cleavage site. Review of mammalian HYAL4s shows that they all possess GPI cleavage sites at the same position; i.e., a relatively serine-rich domain from residues 456-464 (see, e.g., Exhibits A-G, where a serine-glycine pair flanks the cleavage site[1]). Further, the active site or Glyco-hydro-56 family domain structure[2] for HYAL4 is also known (i.e., from residues 41 to 373; see Exhibits A-G). Thus, one of skill in the art would know the sequences for the minimal components that make-up the CHASEGP as claimed, including sequences which define the chondroitinase domain and the minimum length for C-terminal truncation.

Regarding the 70% identity element, claim 1 (from which claim 12 depends) recites that the CHASEGP portion of the polypeptide consists essentially of the chondroitinase domain of the HYAL4 polypeptide or a catalytically active portion thereof. In view of the above, for the chondroitinase domain that would, at minimum, include at least residues 41 to 373 of any of the mammalian HYAL4 species, which amino acid residues making up this region are relatively invariant (compare Exhibits A-G). Further, as with SEQ ID NO:6, all mammalian HYAL4 sequences have a relatively invariant sequence from residues 35 to 457, which defines the catalytic domain (compare, SEQ ID NO:6 and Exhibits A-G). However, the nucleic acid sequences encoding these domains for naturally occurring mammalian HYAL4 sequences can

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[1] See, e.g., Moran and Caras, J Cell Biol (1991) 115:329-336.

differ by as much as 16% compared to SEQ ID NO:5 (e.g., at least 84% of the full length of SEQ ID NO: 5, which is at least 70%; see, e.g., Exhibit H). Therefore, based on the sequence information available at the time of filing, one of skill in the art could certainly make and use sequences having a greater number of degenerate codons to achieve the invention as claimed in the absence of undue experimentation.

While it is appropriate to recognize variability in determining the scope of invention, determination of what is needed to support generic claims to biological subject matter depends on a variety of factors including 1) knowledge in the particular field, 2) the extent and content of the prior art, 3) the maturity of the science or technology, and 4) the predictability of the aspect at issue. Capon v. Eshhar, 76 U.S.P.Q.2d 1078, 1084, 418 F.3d 1349, at 1356 (Fed. Cir. 2005).

The present invention represents more than "a mere germ of an idea," the specification supplies the novel aspects of the invention, and isolation, characterization and use of chondroitinase glycoproteins are certainly not in the early stages of development (e.g., paragraph [0006]-[0010]). (See, also, Genentech, Inc. v. Novo Nordisk, 42 U.S.P.Q.2d 101, 108 F.3d 1361 (Fed. Cir. 1997)). Further, in the present specification, not only are the general teachings of how to isolate and characterize the CHASEGP provided (e.g., paragraphs [0151] to [0208]), but also specific examples are provided for the production of the truncated form of the molecule (e.g., Example 4, paragraphs [0351]-[0353]). Moreover, while such procedures involve some level of technical manipulation, because such methods and steps are routinely used in the art, such procedures do not rise to the level of undue experimentation. (See, e.g., Johns Hopkins University v. Cellpro, Inc., 47 U.S.P.Q.2d 1705, 152 F.3d 1342 (Fed. Cir. 1998), where the court stated that "experimentation does not constitute undue experimentation" where "it is merely routine.").

Regarding the Wands factors, 1) the breadth of the claims is not such that any and all chondroitinase glycoproteins having any and all sequences are embraced by the claims; 2) as stated above, given the availability of mammalian sequences encoding HYAL4, and relative

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[2] See, e.g., < http://www.ncbi.nlm.nih.gov/sites/entrez?db=cdd&cmd=search&term=hyaluronidase>, last visited June 24, 2008.

domain invariability, procedures involved to identify chondroitinase glycoproteins having the appropriate structures would in fact be routine; 3) the level of skill in the art is high, and such a skilled artisan would have the knowledge and capabilities of using the information provided in the specification, coupled with what was known in the art at the time the invention was filed, to practice the invention commensurate in scope with the amended claims (e.g., one of skill in the art could make and use artificial sequences having a number of degenerate codons to achieve the invention as claimed in the absence of undue experimentation); 4) regarding unpredictability, it is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize the generic invention (see, e.g., In re Angstadt, 537 F.2d 498, 504 (CCPA 1976), accordingly, generic inventions are not *per se* invalid because success for each possible iteration is not assured (see, Capon, at 1357); 5) the specification provides examples of at least three nucleic acid sequences (from two separate mammalian species), including a truncated form of the CHASEGP (see Examples 3 and 4); 6) as stated above, standardized methods for isolating and cloning the CHASEGPs embraced by the claims are disclosed to provide direction to the skilled artisan (e.g., paragraphs [0151]-[0208]); 7) working examples of cloning and expression of the CHASEGP as claimed are disclosed (see Examples 3 and 4); and 8) as stated above, the procedures used to practice the invention are merely routine (e.g., see paragraphs [0151]-[0208] and Examples 3 and 4), and such procedures do not rise to the level of undue experimentation.

Therefore, the claims are enabled because the specification provides appropriate guidance, working examples, and prediction of function based on observed properties of the claimed polypeptide such that one of skill in the art could practice the invention as claimed, in the absence of undue experimentation.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Rejection Under 35 U.S.C. §102

Claims 1, 4-9, 12-15, 22, and 50 stand rejected under 35 U.S.C. §102(e), as allegedly being anticipated by Bodary et al.

Applicants traverse the rejection as applied to the amended claims, including claims dependent therefrom, for the reasons given below. As claims 9,15 and 22 have been canceled, the rejection as applied to this claim is rendered moot.

The Office Action alleges, in pertinent part, that the cited reference teaches the "a protein that is 100% identical to the SEQ ID NO: 6 of the instant application (see sequence alignment), inherently a chondroitinase glycoprotein." However, review of the sequence alignment shows that the reference does not teach SEQ ID NO:6, and in fact, Bodary et al. teach a sequence that is 481 amino acids long, which is full length HYAL4 (see, e.g., paragraph [0349] of the instant application) which is not the soluble sequence as claimed (see Applicant's specification [0237]). SEQ ID NO:6 is 423 amino acids long, which sets forth the chondroitinase domain, and is truncated at the C-terminal within 7 amino acids of the endogenous GPI cleavage site (see Example 4 and SEQ ID NO:6). Thus, the reference does not meet these elements of the claims.

Further, while the nucleic acid sequence of the Bodary et al. reference may or may not hybridize to SEQ ID NO:3 or SEQ ID NO:5 under the conditions as recited, this fact would not inherently disclose or suggest the CHASEGP as claimed since the nucleic acid of Bodary et al. would not encode a product which comprises a HYAL polypeptide that is truncated at the C-terminal terminus, nor is it soluble, as required in the present claims.

As stated in Hybritech Inc. v. Monoclonal Antibody, Inc., 231 USPQ 81 (Fed. Cir. 1986), "It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention."

Therefore, because the instant claims recite a glycoprotein comprising a HYAL4 which is truncated at the C-terminal, Bodary et al. do not anticipate the claimed invention.

Failure of the prior art to meet every element of the claimed invention does not meet the standard under §102. For these reasons, Applicants respectfully request that the rejection be withdrawn.

Conclusion

Applicants submit that pending claims 1, 3-10, 12-14, 16, 22, and 50 are in condition for allowance. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this submission.

Please charge Deposit Account 07-1896 in the amount of $525.00 for a Three Month Extension of Time. The Commissioner is hereby authorized to charge any additional fees required by this submission, or make any credits or overpayments, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,

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